

SEQUENCE LISTING

(1) GENERAL INFORMATION:

(i) APPLICANT: Madison, Edwin L

(ii) TITLE OF INVENTION: TISSUE TYPE PLASMINOGEN ACTIVATOR (t-PA)
VARIANTS HAVING ZYMOGEN CHARACTERISTICS: COMPOSITIONS AND
METHODS OF USE

(iii) NUMBER OF SEQUENCES: 1

(iv) CORRESPONDENCE ADDRESS:

(A) ADDRESSEE: McDonnell Boehnen Hulbert & Berghoff
(B) STREET: 300 South Wacker Drive, 32nd Floor
(C) CITY: Chicago
(D) STATE: IL
(E) COUNTRY: USA
(F) ZIP: 60606

(v) COMPUTER READABLE FORM:

(A) MEDIUM TYPE: Floppy disk
(B) COMPUTER: IBM PC compatible
(C) OPERATING SYSTEM: PC-DOS/MS-DOS
(D) SOFTWARE: PatentIn Release #1.0, Version #1.30

(vi) CURRENT APPLICATION DATA:

(A) APPLICATION NUMBER:
(B) FILING DATE:
(C) CLASSIFICATION:

(viii) ATTORNEY/AGENT INFORMATION:

(A) NAME: Zimmerman, Roger P
(B) REGISTRATION NUMBER: 38,670
(C) REFERENCE/DOCKET NUMBER: 97,707

(ix) TELECOMMUNICATION INFORMATION:

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(B) TELEFAX: 312-913-0002

(2) INFORMATION FOR SEQ ID NO:1:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 527 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: not relevant
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: peptide

(iii) HYPOTHETICAL: NO

(iv) ANTI-SENSE: NO

(vi) ORIGINAL SOURCE:

(A) ORGANISM: Homo sapiens

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:1:

5	Ser Tyr Gln Val Ile Cys Arg Asp Glu Lys Thr Gln Met Ile Tyr Gln	1 5 10 15
	Gln His Gln Ser Trp Leu Arg Pro Val Leu Arg Ser Asn Arg Val Glu	20 25 30
10	Tyr Cys Trp Cys Asn Ser Gly Arg Ala Gln Cys His Ser Val Pro Val	35 40 45
	Lys Ser Cys Ser Glu Pro Arg Cys Phe Asn Gly Gly Thr Cys Gln Gln	50 55 60
15	Ala Leu Tyr Phe Ser Asp Phe Val Cys Gln Cys Pro Glu Gly Phe Ala	65 70 75 80
	Gly Lys Cys Cys Glu Ile Asp Thr Arg Ala Thr Cys Tyr Glu Asp Gln	85 90 95
20	Gly Ile Ser Tyr Arg Gly Thr Trp Ser Thr Ala Glu Ser Gly Ala Glu	100 105 110
25	Cys Thr Asn Trp Asn Ser Ser Ala Leu Ala Gln Lys Pro Tyr Ser Gly	115 120 125
	Arg Arg Pro Asp Ala Ile Arg Leu Gly Leu Gly Asn His Asn Tyr Cys	130 135 140
30	Arg Asn Pro Asp Arg Asp Ser Lys Pro Trp Cys Tyr Val Phe Lys Ala	145 150 155 160
	Gly Lys Tyr Ser Ser Glu Phe Cys Ser Thr Pro Ala Cys Ser Glu Gly	165 170 175
35	Asn Ser Asp Cys Tyr Phe Gly Asn Gly Ser Ala Tyr Arg Gly Thr His	180 185 190
40	Ser Leu Thr Glu Ser Gly Ala Ser Cys Leu Pro Trp Asn Ser Met Ile	195 200 205
	Leu Ile Gly Lys Val Tyr Thr Ala Gln Asn Pro Ser Ala Gln Ala Leu	210 215 220
45	Gly Leu Gly Lys His Asn Tyr Cys Arg Asn Pro Asp Gly Asp Ala Lys	225 230 235 240
	Pro Trp Cys His Val Leu Lys Asn Arg Arg Leu Thr Trp Glu Tyr Cys	245 250 255
50	Asp Val Pro Ser Cys Ser Thr Cys Gly Leu Arg Gln Tyr Ser Gln Pro	260 265 270
55	Gln Phe Glu Ile Lys Gly Gly Leu Phe Ala Asp Ile Ala Ser His Pro	275 280 285
	Trp Gln Ala Ala Ile Phe Ala Lys His Arg Arg Ser Pro Gly Glu Arg	

	290					295					300					
5	Phe 305	Leu	Cys	Gly	Gly 310	Ile	Leu	Ile	Ser	Ser	Cys 315	Trp	Ile	Leu	Ser	Ala 320
	Ala	His	Cys	Phe	Gln 325	Glu	Arg	Phe	Pro	Pro 330	His	His	Leu	Thr	Val 335	Ile
10	Leu	Gly	Arg	Thr 340	Tyr	Arg	Val	Val	Pro 345	Gly	Glu	Glu	Glu	Gln 350	Lys	Phe
	Glu	Val	Glu 355	Lys	Tyr	Ile	Val	His 360	Lys	Glu	Phe	Asp	Asp 365	Asp	Thr	Tyr
15	Asp	Asn 370	Asp	Ile	Ala	Leu	Leu 375	Gln	Leu	Lys	Ser	Asp 380	Ser	Ser	Arg	Cys
	Ala 385	Gln	Glu	Ser	Ser	Val 390	Val	Arg	Thr	Val	Cys 395	Leu	Pro	Pro	Ala	Asp 400
20	Leu	Gln	Leu	Pro	Asp 405	Trp	Thr	Glu	Cys	Glu 410	Leu	Ser	Gly	Tyr	Gly 415	Lys
	Asp	Glu	Ala	Leu 420	Ser	Pro	Phe	Tyr	Ser 425	Glu	Arg	Leu	Lys	Glu 430	Ala	His
25	Val	Arg	Leu 435	Tyr	Pro	Ser	Ser	Arg 440	Cys	Thr	Ser	Gln	His 445	Leu	Leu	Asn
	Arg	Thr 450	Val	Thr	Asp	Asn 455	Met	Leu	Cys	Ala	Gly	Asp 460	Thr	Arg	Ser	Gly
30	Gly 465	Pro	Gln	Ala	Asn 470	Leu	His	Asp	Ala	Cys	Gln 475	Gly	Asp	Ser	Gly	Gly 480
35	Pro	Leu	Val	Cys	Leu 485	Asn	Asp	Gly	Arg	Met 490	Thr	Leu	Val	Gly	Ile 495	Ile
	Ser	Trp	Gly	Leu 500	Gly	Cys	Gly	Gln	Lys 505	Asp	Val	Pro	Gly	Val 510	Tyr	Thr
40	Lys	Val	Thr 515	Asn	Tyr	Leu	Asp	Trp 520	Ile	Arg	Asp	Asn	Met 525	Arg	Pro	

45 2) INFORMATION FOR SEQ ID NO:2:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 527 amino acids

(B) TYPE: amino acid

(C) STRANDEDNESS: not relevant

(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: peptide

(iii) HYPOTHETICAL: NO

(iv) ANTI-SENSE: NO

(vi) ORIGINAL SOURCE:

(A) ORGANISM: Homo sapiens

5 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:2:

Ser Tyr Gln Val Ile Cys Arg Asp Glu Lys Thr Gln Met Ile Tyr Gln
 1 5 10 15
 Gln His Gln Ser Trp Leu Arg Pro Val Leu Arg Ser Asn Arg Val Glu
 20 25 30
 Tyr Cys Trp Cys Asn Ser Gly Arg Ala Gln Cys His Ser Val Pro Val
 35 40 45
 Lys Ser Cys Ser Glu Pro Arg Cys Phe Asn Gly Gly Thr Cys Gln Gln
 50 55 60
 Ala Leu Tyr Phe Ser Asp Phe Val Cys Gln Cys Pro Glu Gly Phe Ala
 65 70 75 80
 Gly Lys Cys Cys Glu Ile Asp Thr Arg Ala Thr Cys Tyr Glu Asp Gln
 85 90 95
 Gly Ile Ser Tyr Arg Gly Thr Trp Ser Thr Ala Glu Ser Gly Ala Glu
 100 105 110
 Cys Thr Asn Trp Asn Ser Ser Ala Leu Ala Gln Lys Pro Tyr Ser Gly
 115 120 125
 Arg Arg Pro Asp Ala Ile Arg Leu Gly Leu Gly Asn His Asn Tyr Cys
 130 135 140
 Arg Asn Pro Asp Arg Asp Ser Lys Pro Trp Cys Tyr Val Phe Lys Ala
 145 150 155 160
 Gly Lys Tyr Ser Ser Glu Phe Cys Ser Thr Pro Ala Cys Ser Glu Gly
 165 170 175
 Asn Ser Asp Cys Tyr Phe Gly Asn Gly Ser Ala Tyr Arg Gly Thr His
 180 185 190
 Ser Leu Thr Glu Ser Gly Ala Ser Cys Leu Pro Trp Asn Ser Met Ile
 195 200 205
 Leu Ile Gly Lys Val Tyr Thr Ala Gln Asn Pro Ser Ala Gln Ala Leu
 210 215 220
 Gly Leu Gly Lys His Asn Tyr Cys Arg Asn Pro Asp Gly Asp Ala Lys
 225 230 235 240
 Pro Trp Cys His Val Leu Lys Asn Arg Arg Leu Thr Trp Glu Tyr Cys
 245 250 255
 Asp Val Pro Ser Cys Ser Thr Cys Gly Leu Arg Gln Tyr Ser Gln Pro
 260 265 270
 Gln Phe Glu Ile Lys Gly Gly Leu Phe Ala Asp Ile Ala Ser His Pro
 275 280 285

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Trp Gln Ala Ala Ile Phe Ala Lys His Arg Arg Ser Pro Gly Glu Arg
 290 295 300
 5 Phe Leu Cys Gly Gly Ile Leu Ile Ser Ser Cys Trp Ile Leu Ser Ala
 305 310 315 320
 Ala His Cys Phe Gln Glu Arg Phe Pro Pro His His Leu Thr Val Ile
 325 330 335
 10 Leu Gly Arg Thr Tyr Arg Val Val Pro Gly Glu Glu Glu Gln Lys Phe
 340 345 350
 15 Glu Val Glu Lys Tyr Ile Val His Lys Glu Phe Asp Asp Asp Thr Tyr
 355 360 365
 Asp Asn Asp Ile Ala Leu Leu Gln Leu Lys Ser Asp Ser Ser Arg Cys
 370 375 380
 20 Ala Gln Glu Ser Ser Val Val Arg Thr Val Cys Leu Pro Pro Ala Asp
 385 390 395 400
 Leu Gln Leu Pro Asp Trp Thr Glu Cys Glu Leu Ser Gly Tyr Gly Lys
 405 410 415
 25 Glu Glu Ala Leu Ser Pro Phe Tyr Ser Glu Arg Leu Lys Glu Ala His
 420 425 430
 Val Arg Leu Tyr Pro Ser Ser Arg Cys Thr Ser Gln His Leu Leu Asn
 435 440 445
 30 Arg Thr Val Thr Asp Asn Met Leu Cys Ala Gly Asp Thr Arg Ser Gly
 450 455 460
 35 Gly Pro Gln Ala Asn Leu His Asp Ala Cys Gln Gly Asp Ser Gly Gly
 465 470 475 480
 Pro Leu Val Cys Leu Asn Asp Gly Arg Met Thr Leu Val Gly Ile Ile
 485 490 495
 40 Ser Trp Gly Leu Gly Cys Gly Gln Lys Asp Val Pro Gly Val Tyr Thr
 500 505 510
 45 Lys Val Thr Asn Tyr Leu Asp Trp Ile Arg Asp Asn Met Arg Pro
 515 520 525

2) INFORMATION FOR SEQ ID NO:3:

- 50 (i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH: 527 amino acids
 (B) TYPE: amino acid
 (C) STRANDEDNESS: not relevant
 (D) TOPOLOGY: not relevant
 55 (ii) MOLECULE TYPE: peptide
 (iii) HYPOTHETICAL: NO

(iv) ANTI-SENSE: NO

(vi) ORIGINAL SOURCE:

(A) ORGANISM: Homo sapiens

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(xi) SEQUENCE DESCRIPTION: SEQ ID NO:3:

10	Ser Tyr Gln Val Ile Cys Arg Asp Glu Lys Thr Gln Met Ile Tyr Gln	1	5	10	15
	Gln His Gln Ser Trp Leu Arg Pro Val Leu Arg Ser Asn Arg Val Glu	20	25	30	
15	Tyr Cys Trp Cys Asn Ser Gly Arg Ala Gln Cys His Ser Val Pro Val	35	40	45	
	Lys Ser Cys Ser Glu Pro Arg Cys Phe Asn Gly Gly Thr Cys Gln Gln	50	55	60	
20	Ala Leu Tyr Phe Ser Asp Phe Val Cys Gln Cys Pro Glu Gly Phe Ala	65	70	75	80
	Gly Lys Cys Cys Glu Ile Asp Thr Arg Ala Thr Cys Tyr Glu Asp Gln	85	90	95	
25	Gly Ile Ser Tyr Arg Gly Thr Trp Ser Thr Ala Glu Ser Gly Ala Glu	100	105	110	
30	Cys Thr Asn Trp Asn Ser Ser Ala Leu Ala Gln Lys Pro Tyr Ser Gly	115	120	125	
	Arg Arg Pro Asp Ala Ile Arg Leu Gly Leu Gly Asn His Asn Tyr Cys	130	135	140	
35	Arg Asn Pro Asp Arg Asp Ser Lys Pro Trp Cys Tyr Val Phe Lys Ala	145	150	155	160
	Gly Lys Tyr Ser Ser Glu Phe Cys Ser Thr Pro Ala Cys Ser Glu Gly	165	170	175	
40	Asn Ser Asp Cys Tyr Phe Gly Asn Gly Ser Ala Tyr Arg Gly Thr His	180	185	190	
45	Ser Leu Thr Glu Ser Gly Ala Ser Cys Leu Pro Trp Asn Ser Met Ile	195	200	205	
	Leu Ile Gly Lys Val Tyr Thr Ala Gln Asn Pro Ser Ala Gln Ala Leu	210	215	220	
50	Gly Leu Gly Lys His Asn Tyr Cys Arg Asn Pro Asp Gly Asp Ala Lys	225	230	235	240
	Pro Trp Cys His Val Leu Lys Asn Arg Arg Leu Thr Trp Glu Tyr Cys	245	250	255	
55	Asp Val Pro Ser Cys Ser Thr Cys Gly Leu Arg Gln Tyr Ser Gln Pro	260	265	270	

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Gln Phe Glu Ile Lys Gly Gly Leu Phe Ala Asp Ile Ala Ser His Pro
 275 280 285
 5 Trp Gln Ala Ala Ile Phe Ala Lys His Arg Arg Ser Pro Gly Glu Arg
 290 295 300
 Phe Leu Cys Gly Gly Ile Leu Ile Ser Ser Cys Trp Ile Leu Ser Ala
 305 310 315 320
 10 Ala His Cys Phe Gln Glu Arg Phe Pro Pro His His Leu Thr Val Ile
 325 330 335
 Leu Gly Arg Thr Tyr Arg Val Val Pro Gly Glu Glu Glu Gln Lys Phe
 15 340 345 350
 Glu Val Glu Lys Tyr Ile Val His Lys Glu Phe Asp Asp Asp Thr Tyr
 355 360 365
 20 Asp Asn Asp Ile Ala Leu Leu Gln Leu Lys Ser Asp Ser Ser Arg Cys
 370 375 380
 Ala Gln Glu Ser Ser Val Val Arg Thr Val Cys Leu Pro Pro Ala Asp
 385 390 395 400
 25 Leu Gln Leu Pro Asp Trp Thr Glu Cys Glu Leu Ser Gly Tyr Gly Lys
 405 410 415
 His Glu Ala Leu Ser Pro Phe Tyr Ser Glu Arg Leu Tyr Glu Ala His
 30 420 425 430
 Val Arg Leu Tyr Pro Ser Ser Arg Cys Thr Ser Gln His Leu Leu Asn
 435 440 445
 35 Arg Thr Val Thr Asp Asn Met Leu Cys Ala Gly Asp Thr Arg Ser Gly
 450 455 460
 Gly Pro Gln Ala Asn Leu His Asp Ala Cys Gln Gly Asp Ser Gly Gly
 465 470 475 480
 40 Pro Leu Val Cys Leu Asn Asp Gly Arg Met Thr Leu Val Gly Ile Ile
 485 490 495
 Ser Trp Gly Leu Gly Cys Gly Gln Lys Asp Val Pro Gly Val Tyr Thr
 45 500 505 510
 Lys Val Thr Asn Tyr Leu Asp Trp Ile Arg Asp Asn Met Arg Pro
 515 520 525

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(2) INFORMATION FOR SEQ ID NO:4:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 290 base pairs

(B) TYPE: nucleic acid

(C) STRANDEDNESS: not relevant

(D) TOPOLOGY: not relevant

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(ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

(iv) ANTI-SENSE: NO

(vi) ORIGINAL SOURCE:

(A) ORGANISM: Homo sapiens

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:4:

CTACGGCAAG	CATGAGGCCT	TGTCTCCTTT	CTATTCGGAG	CGGCTGAAGG	AGGCTCATGT	60
CAGACTGTAC	CCATCCAGCC	GCTGCACATC	ACAACATTTA	CTTAACAGAA	CAGTCACCGA	120
CAACATGCTG	TGTGCTGGAG	ACACTCGGAG	CGGCGGGCCC	CAGGCAAAC	TGCACGACGC	180
CTGCCAGGGC	GATTCGGGAG	GCCCCCTGGT	GTGTCTGAAC	GATGGCCGCA	TGACTTTGGT	240
GGGCATCATC	AGCTGGGGCC	TGGGCTGTGG	ACAGAAGGAT	GTCCCGGGTG		290

(2) INFORMATION FOR SEQ ID NO:5:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 290 base pairs

(B) TYPE: nucleic acid

(C) STRANDEDNESS: not relevant

(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

(iv) ANTI-SENSE: NO

(vi) ORIGINAL SOURCE:

(A) ORGANISM: Homo sapiens

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:5:

CTACGGCAAG	GACGAGGCCT	TGTCTCCTTT	CTATTCGGAG	CGGCTGAAGG	AGGCTCATGT	60
CAGACTGTAC	CCATCCAGCC	GCTGCACATC	ACAACATTTA	CTTAACAGAA	CAGTCACCGA	120
CAACATGCTG	TGTGCTGGAG	ACACTCGGAG	CGGCGGGCCC	CAGGCAAAC	TGCACGACGC	180
CTGCCAGGGC	GATTCGGGAG	GCCCCCTGGT	GTGTCTGAAC	GATGGCCGCA	TGACTTTGGT	240
GGGCATCATC	AGCTGGGGCC	TGGGCTGTGG	ACAGAAGGAT	GTCCCGGGTG		290

(2) INFORMATION FOR SEQ ID NO:6:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 290 base pairs

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- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: not relevant
- (D) TOPOLOGY: not relevant

5 (ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

(iv) ANTI-SENSE: NO

10

(vi) ORIGINAL SOURCE:

(A) ORGANISM: Homo sapiens

15

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:6:

CTACGGCAAG	GAGGAGGCCT	TGTCTCCTTT	CTATTCGGAG	CGGCTGAAGG	AGGCTCATGT	60
20	CAGACTGTAC	CCATCCAGCC	GCTGCACATC	ACAACATTTA	CTTAACAGAA	120
	CAACATGCTG	TGTGCTGGAG	ACACTCGGAG	CGGCGGGCCC	CAGGCAAAC	180
	CTGCCAGGGC	GATTCGGGAG	GCCCCCTGGT	GTGTCTGAAC	GATGGCCGCA	240
25	GGGCATC	ATCAGCTGGGGCC	TGGGCTGTGG	ACAGAAGGAT	GTCCCGGGTG	290

(2) INFORMATION FOR SEQ ID NO:7:

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(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 290 base pairs

(B) TYPE: nucleic acid

(C) STRANDEDNESS: not relevant

35

(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

40

(iv) ANTI-SENSE: NO

(vi) ORIGINAL SOURCE:

(A) ORGANISM: Homo sapiens

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(xi) SEQUENCE DESCRIPTION: SEQ ID NO:7:

50	CTACGGCAAG	CATGAGGCCT	TGTCTCCTTT	CTATTCGGAG	CGGCTGTATG	AGGCTCATGT	60
	CAGACTGTAC	CCATCCAGCC	GCTGCACATC	ACAACATTTA	CTTAACAGAA	CAGTCACCGA	120
	CAACATGCTG	TGTGCTGGAG	ACACTCGGAG	CGGCGGGCCC	CAGGCAAAC	TGCACGACGC	180
55	CTGCCAGGGC	GATTCGGGAG	GCCCCCTGGT	GTGTCTGAAC	GATGGCCGCA	TGACTTTGGT	240
	GGGCATC	ATCAGCTGGGGCC	TGGGCTGTGG	ACAGAAGGAT	GTCCCGGGTG		290

(2) INFORMATION FOR SEQ ID NO:8:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 23 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: not relevant
- (D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

(iv) ANTI-SENSE: NO

(vi) ORIGINAL SOURCE:

- (A) ORGANISM: Homo sapiens

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:8:

CTACGGCAAG GACGAGGCCT TGT

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(2) INFORMATION FOR SEQ ID NO:9:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 23 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: not relevant
- (D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

(iv) ANTI-SENSE: NO

(vi) ORIGINAL SOURCE:

- (A) ORGANISM: Homo sapiens

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:9:

CTACGGCAAG GAGGAGGCCT TGT

23

(2) INFORMATION FOR SEQ ID NO:10:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 25 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: not relevant
- (D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

(iv) ANTI-SENSE: NO

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(vi) ORIGINAL SOURCE:

(A) ORGANISM: Homo sapiens

10

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:10:

CGGAGCGGCT GTATGAGGCT MCATGT

25